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Pseudocarcinomatous Invasion in Peutz-Jeghers Polyposis

—Report of a Case—

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INTRODUCTION

Since an intestinal polyposis in association with mucocutaneous pigmentations was first observed by Peutz in 1921 and ten subsequent cases were added by Jeghers[1](1949), numerous cases have been cumulated under the designation of Peutz-Jeghers syndrome. Substantial portions of these cases were once described as having polyps with malignant changes[2~7] which led Peutz-Jeghers polyps to be regarded as one of the premalignant familial polyposis of the intestine. In spite of malignant changes microscopically shown in such cases, extraintestinal metastatic lesions occurred very rarely, and even some malignant cases with metastasis did not provide the solid evidence of carcinomas originating from the Peutz-Jeghers polyps[8,9]. Thus, it is our purpose to present a case of Peutz-Jeghers polyposis manifested with peculiar histology of pseudocarcinomatous glandular and mucinous trapping and to discuss its nature with special emphasis on the differential diagnosis from the genuine malignant change of this polyp.

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CASE HISTORY

A twenty-four years old male patient was admitted to the hospital with the chief complaint of intermittent abdominal pain for 7 months. Six years ago, he had received a segmental resection of the small bowel due to intussusception, but a bout of melena occurred one year prior to this admission. None of family member was found to present either mucocutaneous pigmentations or a history of recurrent abdominal pain. On physical examination, he was chronically ill looking and pale. There were multiple tiny dark brownish pigmentations on palm, sole, oral mucosa and lip. All of the laboratory tests were within normal range except moderate anemia (hemoglobin was 8.6 mg%) and positive HBsAg. Sigmoidoscopy and colonofiberscopy demonstrated multiple sessile and pedunculated polyps. Barium contrast radiographic studies of the alimentary tract revealed multiple filling defects in both jejunum and rectosigmoid areas and delayed barium passage.

On operation, the peritoneal cavity showed mild adhesion due to the previous surgery. There were seven foci of intussusception in jejunum, the largest one of which was located 1 meter proximal to the

ileocecal valve. A Meckel's diverticulum was found 60 cm proximal to the ileocecal valve along the antimesenteric border measuring 4 cm in length and 3 cm in diameter. A segment of jejunum about 1 meter length was resected and Meckel's diverticulum was removed. The patient recovered uneventfully. Follow-up sigmoidoscopy demonstrated stationary condition of the remained rectosigmoid polyps.

PATHOLOGIC FINDINGS

The resected segment of small intestine was 82 cm in length and 9 cm in average circumference. There were 43 polypoid tumors on the mucosal surface of the intestine scatteredly, and the largest one measured 4×3×2.5 cm with 4 cm long stalk. Numerous small sessile polyps of less than 0.5cm in diameter were scattered all over the entire mucosa (Fig. 1 and 2). The cut surface of the polyps were tanwhite, firmand partly lobulated. The serosal surface showed multifocal subserosal hemorrhage probably in relation with intussusception.

Histologically, the polyps consisted of two components: the bulk of epithelial element and smooth muscle bundle. Epithelial component in the polyps was supported by the framework of the branching and/or arborizing bands of smooth muscle fibers which were broader at the center of the tumors and became thinner towards the periphery (Fig. 5). The glands of the epithelium rested on these branching smooth muscle bundles in the same manner as they are in the muscularis mucosa of normal mucous membrane. And also they were surrounded by a delicate connective tissue stroma identical to the normal lamina propria, containing small amount of mature lymphocytes. The Paneth cells, goblet cells and argentaffin cells congregated at the base of the glands next to the muscular framework in the exactly same way as they were located around the base of the crypt of Lieberkuehn of normal intestine (Fig. 5). The epithelial and connective tissue components covered the branching bands of smooth muscle as in normal mucosa, and the epithelial cells were arranged normally and identical to the normal mucosal cell proportion. However the composition cells were devoid of nuclear hyperchromatism, increased mitotic figures or any other evidence of dedifferentiation. The adjacent small intestinal mucosa was unremarkable except some stigma of the intussusception.

A focus of subserosal elevation with fibrosis was found on the opposite serosal surface of a sessile polyp which measured 1.2×1.0 cm at 40 cm distal to the proximal resection margin. This focus corresponded microscopically to the area of pseudoinvasive glandular structures where the original muscle coat was disrupted and multiple mucin pools were entrapped. The submucosa was the seat of granulation tissue formation (Fig. 3 and 4). Those findings were resembling the mucinous adenocarcinoma invading the muscle layer. The nuclei of the entrapped glandular epithelium within the muscle coat were slightly hyperchromatic and less regularly arranged, and mucin pools were formed by the secretory epithelial cells, but lined in part by same nature of hamartomatous epithelial cells (Fig. 6). The mucinous substance was irregularly condensed and often mature mucinophages were entrapped. This type of mucin pools were rarely scattered within the hamartomatous mucosal folds as well. However, tissue fragments or signet ring cells were not found in the inspissated mucin collection. The overlying polyp was not different from the other hamartomatous polyp microscopically.

COMMENT

The case presented is characterized by multiple intestinal hamartomatous polyps and mucocutaneous melanin pigmentations with no family history, but still sufficient to meet its diagnostic criteria of Peutz-Jeghers syndrome[5,10~13]. Not all of the three features occur concurrently or are present in every case. Our major concern is to clarify the nature of a polypoid lesion whether this indicates a carcino-

matous invasion arising from the Peutz-Jeghers polyp or merely represents a Peutz-Jeghers polyp with some peculiar pseudoinvasive growth into the muscle layer and subserosa. Although our case resembles infiltrative growth of the epithelial elements into the muscle layer, the followings are helpful to eliminate the possibility of carcinoma; first of all, entrapped cells in the proper muscle layer consisted of mixture of secreting, Paneth, absorptive and argentaffin cells throughout. Existence of such an admixture of various cell types is an unusual finding of adenocarcinoma. Nuclei of the lining cells appeared somewhat hyperchromatic and exhibited a few mitotic figures, but those may also reflect the irritation sign of benign structure by repeated episodes of intussusception. The irregular distribution of the mucinous cysts and glands in the muscle layer is also different from the uniform pattern of adenocarcinomatous invasion. Presence of mucin pools in gastrointestinal polypoid neoplasms requires an attention on mucinous adenocarcinoma or malignant potentiality. Generally, floating of tumor cells within the mucin pool is a typical morphology of mucinous adenocarcinoma, while in our case mucinous substance appears brand acellular and contains only benign mucinophages, indicating strongly the phenomenon with oversecretion of mucin which becomes trapped between mucosal folds in the polyps by repeated bout of intussusception, and subsequently made chance of misplacing irritated glandular structures[14]. This assumption is supported by the localized granulation tissue formation along the serosal surface of the pseudocarcinomatous area.

It has been clearly documented that carcinoma may arise from the gastrointestinal polyps in Peutz-Jeghers syndrome with an extreme rarity[11]. In the Bartholemew's series[5] in which were 69 cases mostly from literature review included, as many as 20% of them showed polyps with low grade malignancy in histologic study. Many of previous reports regarded presence of epithelial components entrapped within the muscle bundle and mitotic figures as malignant changes of the Peutz-Jeghers polyps, but extraintestinal metastasis is extremely rare to admit high malignant potentiality of these polyps. Furthermore, metastatic lesions in a few cases[15] were far advanced that it was not clear whether they originated from the Peutz-Jeghers polyps.

Malignant changes of Peutz-Jeghers polyps have been described in 3 out of 13 cases in Korean literatures[16~18], which accounted for 23.1% of Peutz-Jeghers syndrome. None of these three cases showed either matastatic lesion or spreading of tumor into the adjacent organs, and the microscopic descriptions were very similar to those of our case; tumor cells were embedded within the muscle layer and mucin lake. We believe that polyps in the above three cases are not genuine adenocarcinomas but represent pseudoinvasive growth of epithelial elements within the hamartomatous muscle layer.

SUMMARY

A case of Peutz-Jeghers syndrome with pseudocarcinomatous entrapping of tumor epithelium and mucin leakage from a 24 years old male was presented. He had suffered from recurrent intussusceptions and received segmental resection of the small intestine. There were multiple hamartomatous polyps with an area in which were pseudocarcinomatous growth of the glandular elements and mucin leakage entrapped within the distorted muscle layer and extending to the subserosa, where a localized granulation tissue formation was evident. It differed from adenocarcinoma with its absence of cellular atypia, no flank invasive growth and hamartomatous admixture of smooth muscle bundles. It is assumed that repeated bout of intussusceptions may cause oversecretion of mucin which is trapped between mucosal folds and provides chances of glandular misplacement into the muscle bundles.

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=국문초록=

良性腺狀構造의 筋層內 假性侵潤을 보인 Peutz-Jeghers 폴립증

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저자들은 반복되는 腸重疊으로 인해 小腸切除術을 시행받은 24세 남자에서 전형적인 Peutz-Jeghers 폴립증의 病理學的 特性과 함께 粘膜上皮의 筋層內陷入을 관찰하고 이를 보고하였다. 점막층에는 많은 過誤腫性 폴립이 있었으며 그 중 한개에서는 腺構造의 근층내 침윤과 粘液의 粘膜下流出을 동반하였고 이는 漿膜側까지 침범하여 肉芽組織을 형성하였다. 비록 筋層을 침윤하고 있었으나 細胞學的 및 構造的 異型이 없고 平滑筋이 불규칙하게 섞여 있는 점등은 癌腫과는 區別되는 소견이었다. 저자들은 이러한 病變이 반복되는 장중첩에 의해 粘液의 過分泌와 점막의 근층내 陷入되는 과정을 밟는다고 생각하였으며 암종과의 감별점을 토의하였다.

Legends for Figures

Fig. 1. Luminal surface of the resected jejunum. There are 43 polypoid tumors on the mucosal surface of the intestine. The largest one(←) measures 4×3×2.5 cm.

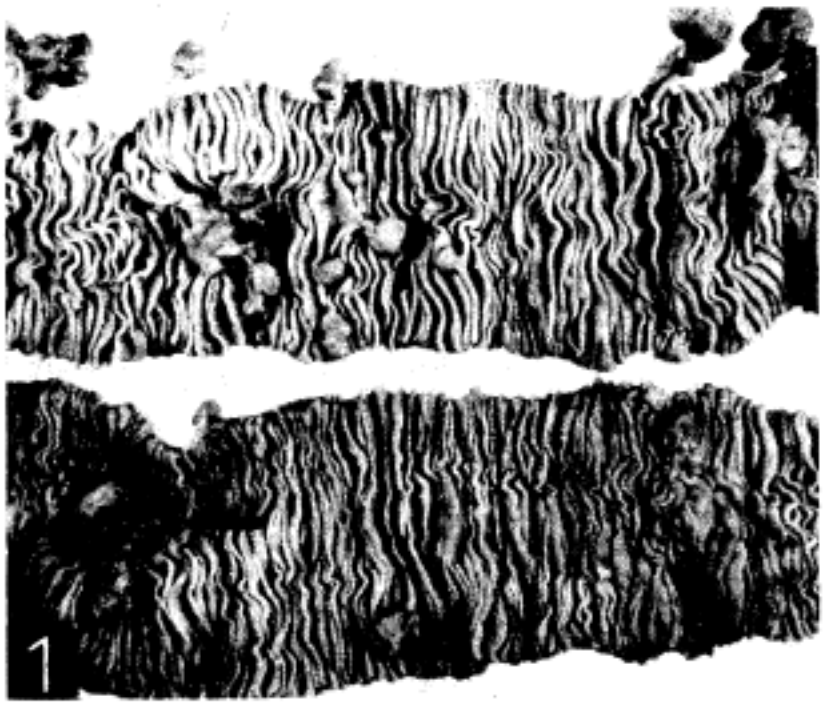
Fig. 2. Close-up view of the resected specimen. The surface of the polyp is granular but lobulated, and most of them have slender stalks.

Fig. 3. Scanning view of a sessile polyp with serosal fibrous plaque. The epithelial component penetrates into the underlying tissue, by which the muscle coat is focally disrupted. Mucin pools around the pseudoinvasive epithelial structure are lined partly by secretory epithelial cells. The serosal surface is made of granulation tissue with mucin leakage. (H&E, ×7)

Fig. 4. Scanning view of another level of the same polyp (Fig. 3). Two large mucin pools are entrapped within the submucosal portion, but one focus shows a misplaced branching gland within the muscle coat (rectangle). (H&E, ×7)

Fig. 5. A representative microscopic feature of the polypoid tumors. The muscle bundles are in arborizing arrangement and the epithelial cells rest on these branding smooth muscle bundles. Epithelial elements consist of absorptive, goblet and occasionally Paneth cells in normal composition. (H&E, ×40).

Fig. 6. The microscopic feature of sessile polyp illustrated in Fig. 3 and 4. The muscle coat is splitted by mucin collection which is continuous with benign epithelial proliferation.(H&E, ×40). Inset is a higher magnification of the rectangle in Fig. 4. The epithelial cells are monotonous, uniformly arranged and normochromic without any evidence of atypicality. (H&E, ×40).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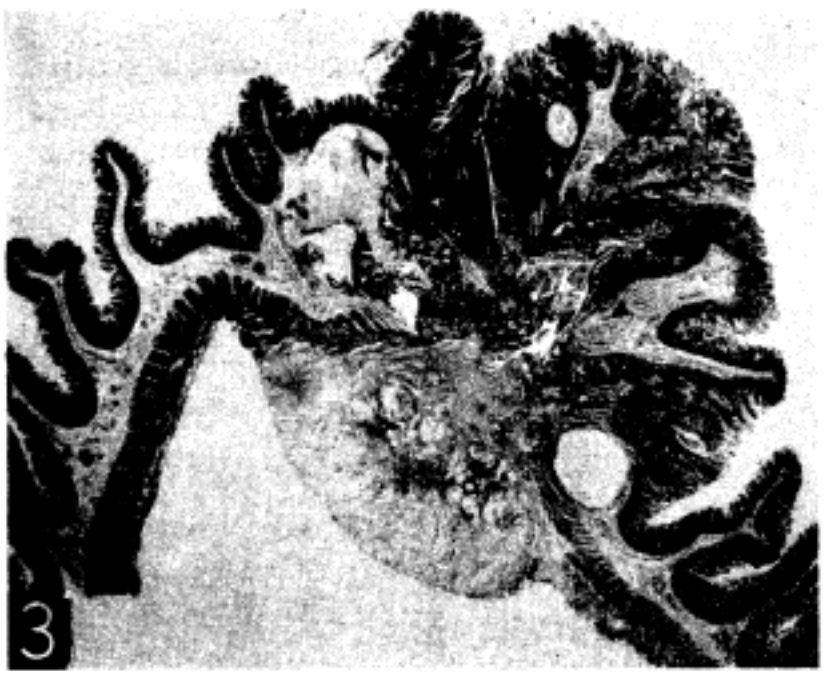
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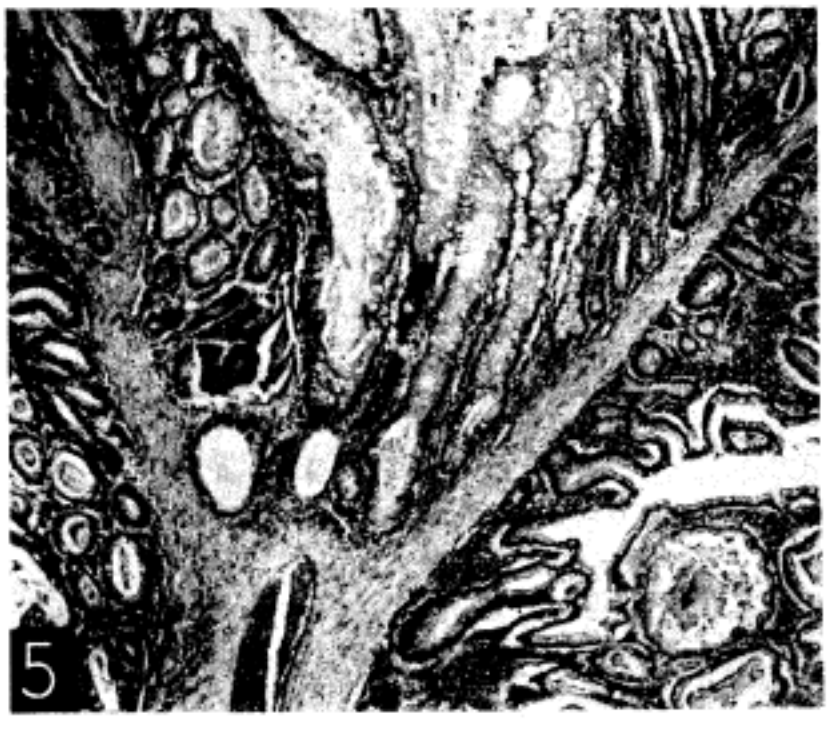
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